THE AUTONOMIC-COGNITION CLINICAL CORRELATION IN INDONESIAN PARKINSON'S DISEASE SUBJECTS

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Abstract

Background: Dysautonomia and cognitive impairment are common in PD, affecting quality of life and disease progression. Understanding their connection enables earlier identification of at-risk patients. This study investigates the correlation between dysautonomia and cognitive impairment in Indonesian PD patients. **Methods and Materials:** This cross-sectional study collected demographic and clinical data, including SCOPA-COG INA and SCOPA-AUT INA. Independent t-tests, Mann-Whitney U tests, Pearson's, and Spearman's correlation tests analyzed associations. **Results**: We recruited 33 PD subjects, primarily male (72.7%) and elderly (63.6%). The median age was 61 years, with 60.6% having a disease duration of at least 5 years and 66.7% at a mild stage. Median levodopa equivalent daily dose (LEDD) was 325 mg. Median SCOPA-COG INA and SCOPA-AUT INA were 24 and 17. Cognitive impairment was present in 45.4%, and dysautonomia in 15.2%. Elderly subjects had lower SCOPA-COG INA (20.19±7.18 vs 27.58±5.98). Cognitively impaired subjects had worse SCOPA-AUT INA (20.6±7.81 vs. 13.89±6.43) and higher LEDD (408.33±140.25 vs. 275.28±134.51). Cognitively impaired subjects had worse SCOPA-AUT INA urinary symptoms ($p<0.05$). No differences were found between subjects with and without dysautonomia or when divided by median SCOPA-AUT INA. SCOPA-COG INA and SCOPA-AUT INA were significantly correlated ($\rho = -0.368$, $p < 0.05$), as were the SCOPA-COG INA memory domain and SCOPA-AUT INA cardiovascular domain ($\rho = 0.399$, $p < 0.05$). **Conclusion:** In Indonesian PD patients, cognitive impairment is significantly correlated with dysautonomia. Age, age at onset, and LEDD were significantly associated with cognitive impairment but not with dysautonomia. Further exploration could enhance understanding of this correlation.

Keywords

Parkinson's disease, cognitive impairment, autonomic dysfunction, SCOPA-COG INA, SCOPA-AUT INA

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease following Alzheimer's disease.[1] The World Health Organization (WHO) stated that, in 2019, over 8.5 million people have been diagnosed with PD.[2] PD also has a rise of 81% in disease-adjusted life years (DALY) from 2000 to 2019 while simultaneously causing 329,000 deaths.[2] A recent study in 2024 found that 1.51 in 1,000 people in the world were diagnosed with PD, increasing from 1.1 in 1,000 people in 2019.[1] Approximately ten new PD cases in Indonesia are diagnosed annually, with an estimated prevalence of 400,000 patients.[3]

Non-motor symptoms (NMS) in PD have garnered significant attention recently, as evidenced by a bibliometric analysis showing a marked increase in PD-related NMS publications between 2013 and 2022.[4] Gupta and Shukla also considered that NMS is a 'dark horse' regarding the PD disease clinical course that can cause irreversible PD symptoms.[5] The pathogenesis of NMS is believed to involve noradrenergic, glutamatergic, serotonergic, and adenosine pathways, among others, providing a biological foundation for various NMS manifestations, including autonomic dysfunction and cognitive impairment.[6] Several instruments are widely available to assess dysautonomia and cognitive impairment in PD, including the Scale for Outcomes in Parkinson's Disease for Autonomic (SCOPA-AUT) and Cognition (SCOPA-COG) assessments, which has been approved by the Movement Disorder Society (MDS).[7,8]

Dysautonomia and cognitive impairment in PD are often missed because it was thought to be an aging process, while both symptoms can be used as predictive factors in PD disease progression when identified early.[9-12] Additionally, studies regarding both symptoms in Indonesian PD subjects still need to be completed. The purpose of this study is to describe the characteristics of autonomic dysfunction and cognitive impairment in Indonesian PD subjects and to explore the correlation between both symptoms.

Materials and Methods

This study received ethical approval from the Health Research Ethics Committee (HREC) of the Faculty of Medicine, Universitas Indonesia. Based on Declaration of Helsinki, the informed consent document was developed and subsequently reviewed and approved by the HREC. Upon obtaining ethical clearance, the sample collection phase commenced.

This cross-sectional study took place at the neurology outpatient clinic of Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia, between January and July 2024. We recruited subjects who were attending routine clinical checkups consecutively. The inclusion criteria included (1) subjects with an established PD diagnosis by a neurologist using the criteria from the United Kingdom Parkinson's Disease Society Brain Bank (UKPDSBB)[13], (2) subjects aged 18 years or older, and (3) willingness to participate in the

study. The exclusion criteria included (1) inability to speak and comprehend the Indonesian language and (2) severe speech and/or language disabilities. We determined that a minimum of 30 samples was sufficient, as this number is considered adequate for statistical analysis in exploratory studies.[14]

We collected basic demographic variables, including gender, age, and age at onset of PD. We also gathered clinical variables, such as disease duration, Hoehn and Yahr (H&Y) staging, the MDS revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS), current anti-PD medications, and levodopa equivalent daily dose (LEDD). We assessed SCOPA-AUT INA and SCOPA-COG INA, including subdomains of both instruments. SCOPA-AUT INA is a 23-item self-completed questionnaire that evaluates autonomic dysfunction in PD patients. The 23 items fall into six domains: (1) gastrointestinal functioning (seven items), (2) urinary functioning (six items), (3) cardiovascular functioning (three items), (4) thermoregulatory functioning (four items), (5) pupillomotor functioning (one item), and (6) sexual function (two items for men and two for women). The maximum score is 69, with higher scores indicating worse autonomic performance; each item receives a score from 0 (never experiencing the symptom) to 3 (often experiencing the symptom).[7] In contrast, SCOPA-COG INA is a clinician-rated instrument with ten subtests that evaluate neuropsychological domains commonly affected in cognitively impaired PD patients: (1) attention, (2) memory, (3) executive functions, and (4) visuospatial abilities. Attention tasks include counting and reciting months backwards. Learning and memory are evaluated through word list immediate and delayed recall, spatial span, and digit backward tasks. Executive functions are assessed using alternate hand movements, animal fluency, and a set-shifting task. Visuospatial ability is measured by completing unfinished geometric patterns. The total score ranges from 0 to 43, with lower scores indicating worse cognitive performance.[8]

We divided several variables into subgroups, including gender (male and female), age (≥60 and <60 years), age at onset (<40 and ≥40 years), disease duration (≥5 and <5 years), H&Y staging (mild/H&Y I-II, moderate/H&Y III, and severe/H&Y IV-V), and the number of current anti-PD medications (single/1 drug and multiple/≥1 drug). We also divided the total SCOPA-AUT INA and SCOPA-COG INA scores into subgroups using cutoff scores from previous studies. For SCOPA-AUT INA, no universally agreed cutoff score determines dysautonomia in PD, with prior studies suggesting scores ranging from 9 to 13.1.[15-17] We used a cutoff score of 10, following the most recent study by Martinez-Ramirez et al.[17] Additionally, we used the median score of our study sample to divide the subjects evenly. As for SCOPA-COG INA, we employed established cutoff scores from prior studies to categorize PD subjects into three groups: no cognitive impairment (SCOPA-COG INA 24-43), mild cognitive impairment/PD-MCI (SCOPA-COG INA 17-23), and dementia/PDD (SCOPA-COG INA 0-16).[18,19] According to cutoff point aforementioned above, a score of 23/24 is used to determine whether a PD subject have cognitive impairment or not; a score

of ≥24 is classified as cognitively not impaired, while a score of <24 is classified as cognitively impaired.

We described basic demographic and clinical data using univariate analysis for categorical and continuous variables. We determined the data distribution for continuous variables. In the association analysis, if the continuous dependent variables were normally distributed, we would use independent t-tests; if the continuous dependent variables were not normally distributed, we would use the Mann-Whitney U test. Furthermore, if the dependent variable is identical to the grouped independent variable, it will be excluded as a dependent variable. We also utilized Pearson and Spearman correlation analyses to assess correlations. Spearman correlation analysis would be utilized if any of the continuous variables were not normally distributed. We performed all statistical analyses using SPSS version 29.

Results

In this study, we recruited 33 PD subjects. Among all variables, normal distribution data was found in age, age at onset, LEDD, SCOPA-COG INA total score, and SCOPA-AUT INA total score. Additionally, the executive function subdomain of SCOPA-COG INA and the urinary subdomain of SCOPA-AUT INA also had a normal distribution. Most subjects were male (72.7%) and elderly (63.6%), with a median age of 61 (22-87). Most subjects were at least 40 years old at the onset of the disease (84.8%) and had been experiencing PD symptoms for at least 5 years (60.6%). The majority of subjects had a mild stage of PD (66.7%), determined by the H&Y staging I-II. Most subjects were on levodopa derivatives medication (93.9%) and taking more than one anti-PD medications (81.8%) [Table 1]. The MDS-UPDRS score ranges from 4-126, with a median MDS-UPDRS of 35. LEDD was found to have a score ranging from 0 to 666, with a median LEDD of 325 [Table 2].

Table 1. Univariate analysis of the *categorical* variables from the subjects

Variable	n (%)
Gender	
Male	24 (72.7)
Female	9 (27.3)
Age	
≥60	21 (63.6)
<60	12 (36.4)
Age at onset	
<40	5 (15.2)
≥40	28 (84.8)
Disease duration	
≥5	20 (60.6)
<5	13 (39.4)
Hoehn & Yahr staging	
Mild (HY I-II)	22 (66.7)
Moderate (HY III)	4 (12.1)
Severe (HY IV-V)	7 (21.2)

(contd) Table 1

Variable	n (%)
Anti-PD medication	
Levodopa derivatives	31 (93.9)
Dopamine agonists	23 (69.7)
Anticholinergics	16 (48.5)
Number of current anti-PD medications	
Single anti-PD	6 (18.2)
Multiple anti-PD	27 (81.8)
SCOPA-AUT INA *Cutoff adjusted to 10*	
With dysautonomia (≥10)	5 (15.2)
Without dysautonomia (<10)	28 (84.8)
Cutoff adjusted to 17	
With dysautonomia (≥17)	17 (51.5)
Without dysautonomia (<17)	16 (48.5)
SCOPA-COG INA	
No cognitive impairment (≥24)	18 (54.5)
Mild cognitive impairment (17-23)	8 (24.2)
PD dementia (0-16)	7 (21.2)

Table 2. Univariate analysis of the *continuous* variables from the subjects

Variable	Median (range)
Age[n]	61 (22-87)
Age at onset[n]	56 (16-80)
Disease duration	6 (2-21)
MDS-UPDRS total score	35 (4-126)
Part I	3 (0-24)
Part II	7 (0-38)
Part III	16 (2-56)
Part IV	3 (0-8)
LEDD[n]	325 (0-666)
SCOPA-COG INA total score[n]	24 (7-40)
Memory domain	8 (3-19)
Attention domain	3 (0-4)
Executive function domain[n]	9 (3-12)
Visuospatial domain	3 (0-5)
SCOPA-AUT INA total score[n]	17 (2-32)
GI tract	6 (0-17)
Urinary[n]	6 (0-13)
Cardiovascular	0 (0-6)
Thermoregulatory	2 (0-12)
Pupillomotor	0 (0-3)
Sexual	0 (0-6)

[n] = normally distributed data

The median SCOPA-AUT INA score was 17 (2-32), with a mean score of 16.94±7.76. Among the SCOPA-AUT INA subdomains, gastrointestinal tract and urinary symptoms had the highest median score (6 [0-17]; 6 [0-13]). Using the cutoff score by Martinez-Ramirez et al.[17], most subjects have dysautonomia (84.8%), and when using the median SCOPA-AUT INA score in this study as a cutoff point, most subjects also had dysautonomia (51.5%). In the SCOPA-COG INA assessment, we found a median score of 24 (7-40) and a mean score of 22.88±7.59. Both attention and visuospatial subdomain had the lowest median score (3 [0-4]; 3 [0-5]). Most subjects did not have cognitive impairment (54.5%), with 24.2% and 21.2% classified, respectively, as PD-MCI and PDD [Table 1, Table 2].

Variables with a normal distribution, including age, age at onset, LEDD, SCOPA-COG INA total score, and SCOPA-AUT INA total score, were further analyzed to determine their association with subgroups of categorical variables such as gender, age, age at onset, disease duration, number of current anti-PD medications, presence of cognitive impairment, and presence of dysautonomia. In this study, the age subgroup had a statistically significant association (p = 0.005) with SCOPA-COG INA total score. Specifically, PD subjects who were ≥60 years old showed a lower SCOPA-COG INA total score compared to PD subjects who were <60 years old (20.19±7.18 vs. 27.58±5.98). There was no association between the age subgroup and SCOPA-AUT INA total score. Additionally, the subgroups of gender, age at onset, disease duration, and number of current anti-PD medications did not have a statistically significant association with both SCOPA-COG INA total score and SCOPA-AUT INA total score [Table 3].

Table 3. Independent t-test between normally distributed continuous dependent variables and categoric independent variable

Gender			
Variable	Male n = 24	Female n = 9	p
Age	60.96±11.81	57.11±16.03	.456
Age at onset	53.92±12.14	51.0±15.15	.57
LEDD	335.75±138.41	335.78±189.46	1.00
SCOPA-COG INA total score	22.75±7.71	23.22±7.68	.876
SCOPA-AUT INA total score	16.83±7.85	17.22±7.97	.90
Age			
Variable	≥60 n = 21	<60 n = 12	p
Age at onset	60.52±7.13	40.17±10.02	<.001*
LEDD	348.81±160.51	312.92±135.75	.519
SCOPA-COG INA total score	20.19±7.18	27.58±5.98	.005*
SCOPA-AUT INA total score	18.14±7.16	14.83±8.61	.244
Age at onset			
Variable	<40 n = 5	≥40 n = 28	p
Age	40.2±14.13	63.43±9.18	<.001*
LEDD	343±59.19	334.46±162.56	.909
SCOPA-COG INA total score	27.8±6.94	22±7.47	.117
SCOPA-AUT INA total score	14.6±6.88	17.36±7.95	.473

Disease duration			
Variable	≥5 n = 20	<5 n = 13	p
Age	61.2±13.95	57.92±11.47	.486
Age at onset	51.75±14	55.23±11.03	.456
LEDD	367.95±161.86	286.23±121.57	.13
SCOPA-COG INA total score	21.5±7.59	25±7.37	.20
SCOPA-AUT INA total score	17.4±8.7	16.23±6.31	.679
Number of current anti-PD medications			
Variable	Single anti-PD drugs n = 6	Multiple anti-PD drugs n = 27	p
Age	63.67±10.01	59.07±13.53	.441
Age at onset	57.67±10.11	52.11±13.33	.346
LEDD	299.67±228.76	343.78±132.52	.526
SCOPA-COG INA total score	19.33±7.79	23.67±7.46	.211
SCOPA-AUT INA total score	14±9.02	17.59±7.47	.312

*p<0,05

PD subjects with dysautonomia did not have a statistically significant association with age, age at onset, LEDD, and SCOPA-COG INA total score, either using the cutoff of 10 or 17 [Table 4]. On the other hand, PD subjects with cognitive impairment (SCOPA-COG INA <24) had a statistically significant association with age, age at onset, LEDD, and SCOPA-AUT INA total score. Cognitive-impaired subjects were older (67.8±8.42 vs 53.33±12.5; p = 0.001), older at onset (60.73±8.02 vs 46.78±12.81; p = 0.001), having higher LEDD (408.33±140.25 vs 275.28±134.51; p = 0.009), and having higher SCOPA-AUT INA total score (20.6±7.81 vs 13.89±6.43; p = 0.11) [Table 5]. In a further analysis between the presence of cognitive impairment and SCOPA-AUT INA subdomains, cognitive-impaired subjects only had a statistically significant association with the urinary subdomain of SCOPA-AUT, with cognitive-impaired subjects having higher urinary subdomain score (Mean Rank: 22.1 vs 12.75; p = 0.005) [Table 6].

Table 4. Independent t-test between normally distributed continuous dependent variables and the presence of dysautonomia using the cutoff score of 10 and 17

Variable	**SCOPA-AUT INA ≥10 n = 28**	**SCOPA-AUT INA <10 n = 5**	**p**
Age	60.96±12.74	54±13.91	.275
Age at onset	53.86±12.98	49±12.57	.445
LEDD	351.75±145.41	246.2±165.54	.152
SCOPA-COG INA total score	21.86±7.34	28.6±6.99	.066
Variable	**SCOPA-AUT INA ≥17 n = 17**	**SCOPA-AUT INA <17 n = 16**	**p**
Age	61.35±13.31	58.38±12.79	.518
Age at onset	52.88±13.01	53.38±13.1	.914
LEDD	368.29±149.7	301.19±148.79	.206
SCOPA-COG INA total score	21.59±9.03	24.25±5.65	.316

Table 5. Independent t-test between normally-distributed continuous dependent variables and the presence of cognitive impairment

Variable	Cognitive impairment (+) n = 15	Cognitive impairment (-) n = 18	p
Age	67.8±8.42	53.33±12.5	<.001*
Age at onset	60.73±8.02	46.78±12.81	<.001*
LEDD	408.33±140.25	275.28±134.51	.009*
SCOPA-AUT INA total score	20.6±7.81	13.89±6.43	.011*

* = p<0.05

Table 6. Mann-Whitney U test between SCOPA-AUT INA (including its subdomains) and the presence of cognitive impairment

Variable	Cognitive impairment (+) n = 15	Cognitive impairment (-) n = 18	p
SCOPA-AUT INA total score	20.93	13.72	.033*
GI tract	18.9	15.42	.307
Urinary	22.1	12.75	.005*
Cardiovascular	19.27	15.11	.229
Thermoregulatory	17	17	1.0
Pupillomotor	19.73	14.72	.145
Sexual	15.5	18.25	.421

* = p<0.05

Between normally distributed variables, Pearson correlation analysis showed that SCOPA-AUT INA and SCOPA-COG INA had a statistically significant weak negative correlation (ρ = -0.368; p<0.05). SCOPA-AUT INA had a statistically significant moderate positive correlation with LEDD (ρ = 0.414; p<0.05). SCOPA-COG INA had a clinically significant moderate negative correlation with age (ρ = -0.525; p<0.01) and age at onset (ρ = -0.49; p<0.01) [Table 7]. Using Spearman correlation analysis that also covered both SCOPA-AUT INA and SCOPA-COG INA subdomains, statistically significant correlations were found between SCOPA-AUT INA total score with attention subdomain of SCOPA-COG INA (ρ = -0.439; p<0.05); SCOPA-COG INA total score with the urinary subdomain of SCOPA-AUT INA (ρ = -0.387; p<0.05); cardiovascular subdomain of SCOPA-AUT INA and memory subdomain of SCOPA-COG INA (ρ = 0.399; p<0.05) [Table 8].

Table 7. Pearson correlation matrix table between normally-distributed variables

	Age	Age at onset	LEDD	SCOPA-AUT INA total score	SCOPA-COG INA total score
Age	1				
Age at onset	0.93**	1			
LEDD	0.23	0.114	1		
SCOPA-AUT INA total score	0.30	0.222	0.414*	1	
SCOPA-COG INA total score	-0.525**	-0.49**	-0.263	-0.368*	1

* = p<0.05; ** = p<0.01

Table 8. Spearman correlation matrix table between SCOPA-COG INA and SCOPA-AUT INA (including both instruments' subdomains)

		SCOPA-COG INA				
		Memory	Attention	Executive	Visuo-spatial	TOTAL SCORE
SCOPA-AUT INA	GIT	-0.084	-0.306	-0.096	-0.095	-0.174
	Urinary	-0.23	-0.221	-0.334	-0.226	-0.387*
	Cardio-vascular	0.399*	-0.273	-0.191	-0.128	-0.335
	Thermo-regulatory	-0.082	-0.211	-0.05	0.015	-0.103
	Pupilomotor	-0.281	-0.246	0.046	-0.086	-0.248
	Sexual	0.086	0.03	0.181	0.152	0.121
	TOTAL SCORE	-0.312	-0.439*	-0.237	-0.155	-0.392*

* = p<0.05; ** = p<0.01

Discussion

The subjects in this study overall fit the characteristics found in previous studies, mostly consisting of males, having a disease duration exceeding five years, and mostly at the mild stage. Globally, the average age of individuals with PD exceeds 55 years old, with males being more frequently affected, as evidenced by a male-to-female ratio of 1.5:1.[3,20,21] Similarly, studies focusing on the Indonesian population have also reported that most PD subjects were elderly males.[22-32] Studies from Pagano et al. and Raket et al. observed that

PD onset predominantly occurred in older adults.[33,34] Likewise, Larasanti et al. demonstrated similar trends among Indonesian PD subjects.[27] Previous research has generally reported a disease duration of more than five years in PD patients.[35,36] However, not all studies conducted in Indonesia identified the same findings.[22,23,26-29] Previous studies on the Indonesian population also found the mild stage to be most prevalent.[23,30,31,37,38] Our study observed a median MDS-UPDRS score of 35 (4-126). This is comparable to other studies that reported mean MDS-UPDRS scores ranging from 27.6 to 42.96. Notably, an Indonesian study recorded a mean MDS-UPDRS score of 35.11±21.39.[27,39,40]

In terms of medication profile, we focused on three mainly available anti-PD drugs worldwide and also in Indonesia, which are levodopa-based preparations, dopamine agonists, and anticholinergics.[41,42] In Japan, levodopa-based preparations and non-ergot dopamine agonists were the most prescribed anti-Parkinsonian medications (85.4 and 30.4 respectively), while anticholinergics were only prescribed in 12.7% of the Japanese patients.[43] Heidiyana et al. reported the same finding with our study that most PD subjects were taking multiple anti-PD medications.[31] This difference might be attributable to variations in population characteristics between study locations and temporal differences at the time of data collection.

Our study reported a SCOPA-AUT INA mean score of 16.94±7.76 and a median score of 17 (2–32), which is slightly higher than findings from earlier studies, where mean SCOPA-AUT scores ranged from 4.16 to 12.85.[39,44,45] Similarly, our median score is higher than that reported in an Indonesian population study, which had a median SCOPA-AUT INA score of 12 (6–19).[25] Variability in these results may arise from cultural differences in interpreting and reporting autonomic symptoms, translation nuances, or the validation process of each language version. Additionally, the population characteristics, including disease severity, comorbidities, and demographic factors, can further contribute to discrepancies. The gastrointestinal (GI) tract and urinary subdomains had the highest median scores, aligning with previous findings.[25] Using a cutoff score of both 10 and 17, most subjects exhibited dysautonomia (84.8%, 51.5%), which is consistent with the original study, which found that more than half did not have dysautonomia.[17]

This study also reported the mean and median SCOPA-COG INA score of 22.88±7.59 and 24 (7-40), with attention and visuospatial subdomain having the lowest score. Park et al. reported relatively similar results with mean SCOPA-COG of 22.40±6.95, while Gryfe et al. reported, in an RCT, that attention and visuospatial subdomain were the lowest-scored subdomains.[46,47] Isella et al. also found that most of the subjects were cognitively normal, followed by PD-MCI and PDD, which is similar with our findings.[19]

The SCOPA-COG INA total score was significantly correlated with age, consistent with previous findings.[46,48,49] Cognitive impairment in PD subjects may result not only from age-related neuropathologies, such as limbic and/or neocortical Lewy pathology, but

also from widespread dopaminergic deficits in the brain, reduced noradrenaline-synthesizing neurons in the locus coeruleus and sympathetic systems, and disruptions in the basal forebrain cholinergic systems.[50] Additionally, cognitively impaired PD subjects have been shown to have higher LEDD.[51] While prior studies have reported that SCOPA-AUT is not correlated with age, other studies have produced conflicting results.[52,53] Overall, our findings contrast with studies suggesting that SCOPA-AUT correlates with age at onset and disease duration, whereas SCOPA-COG is associated with gender, age at onset, and disease duration [33,51,54]. These discrepancies may be attributed to variations in clinical profiles across different studies.

Previous studies have demonstrated a significant correlation between dysautonomia and cognitive impairment.[55-62] Using SCOPA-AUT and SCOPA-COG to assess subjects, researchers also identified a significant negative correlation between the two, with Spearman correlation coefficients ranging from -0.23 to -0.14.[63,64] The primary link between dysautonomia and cognitive impairment is believed to be blood pressure dysregulation, which is preceded by autonomic dysfunction.[57] Prolonged and severe autonomic dysfunction can impair blood pressure regulation, potentially leading to asymptomatic brain ischemia and contributing to white matter hyperintensities (WMHs).[57,65] These WMHs represent underlying demyelination and axonal degeneration, which can profoundly impact cognitive function in healthy older adults and individuals with existing cognitive impairment.[57,65]

In further subdomain analysis, most studies identified the cardiovascular aspect of autonomic function as the domain most strongly correlated with cognitive impairment.[56,58,61] However, in our study, the cardiovascular subdomain of SCOPA-AUT INA showed no correlation with either the cognitive impairment subgroup or the SCOPA-COG INA total score. Interestingly, a significant positive correlation was observed between the cardiovascular subdomain of SCOPA-AUT INA and the memory subdomain of SCOPA-COG INA, a finding that appears counterintuitive. Additionally, the urinary subdomain of SCOPA-AUT was significantly correlated with the SCOPA-COG INA total score, consistent with previous findings.[63] This mixed set of results may be attributed to several factors, including the severity of PD in the subjects, medication effects, subjective biases in reporting, and the small sample size.

Conclusions

This study highlights key aspects of the Indonesian PD population, including the NMS, specifically dysautonomia and cognitive impairment. Overall, our study sample had the same characteristics as previous studies, including other studies on Indonesian PD subjects. We found that dysautonomia and cognitive impairment are correlated. This correlation is crucial for managing PD patients and can be used to predict disease severity in the future.[12]

The limitations of this study are (1) the small sample size, (2) no consensus cutoff score (i.e. SCOPA-AUT), and (3) one-time assessment. Future studies focusing on larger sample sizes, proper cutoff scores of the used instruments, and cohort studies with multiple time points would be necessary. A study design with a high evidence-based level, such as a systematic review or meta-analysis, especially in Indonesian populations, would be crucial.

Competing Interests

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript, and there is no financial interest to report.

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